UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC
SUBSTANCES

NOV 13 2012

MEMORANDUM

SUBJECT: Review of the Registrant's response to the deficiencies found by the Agency in its review of product chemistry, manufacturing process, and acute toxicity studies for the registration of the TGAI *Bt. israelensis* strain SUM-6218.

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THROUGH: John L. Kough, Ph.D., Senior Scientist John L. Kough
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TO: Denise Greenway, Regulatory Action Leader
Microbial Pesticides Branch,
Biopesticides and Pollution Prevention Division (7511C)

ACTION REQUESTED: To review the Registrant's response (dated 09/27/2012) to the deficiencies found by the Agency in its review (dated 07/10/2012) of product chemistry, manufacturing process, and acute toxicity studies of the TGAI *Bt. israelensis* strain SUM-6218 (EPA Reg. no. 6218-IG)

CONCLUSION: ACCEPTABLE after the registrant has responded to the following deficiencies:

1. The % by weight of the TGAI on the CSF should be corrected to 100.00%.
2. Remove any statement of using any preservatives/ stabilizers or anti caking agents from the manufacturing process.
3. Test production batches of the TGAI for contamination with pathogenic bacteria, particularly for the presence of enteric pathogens.

CONTAINS FIFRA CONFIDENTIAL BUSINESS INFORMATION

DATA REVIEW RECORD

Active Ingredients:	*Bacillus thuringiensis israelensis* strain SUM-6218
Products Name:	Summit Bti MP
Company Name:	Summit Chemical Co.
ID No:	6218-IG
Chemical Number:	6401
Submission Number:	924489
DP Barcode:	406449
MRID No:	Response to Deficiencies

BACKGROUND:

The registrant has submitted an application for section 3 registration of the TGAI *Bt. israelensis* strain SUM-6218. The following deficiencies were found by the Agency in the application:

1) The product name and active ingredient content are made to match exactly on the CSF and product label.
2) The deposition of the strain in a recognized microbial culture collection is finalized.
3) The CSF is revised to give a minimum spore or cfu content per unit weight, or a minimum potency in ITU/mg.
4) The information on how the seed culture of *Bacillus thuringiensis israelensis* strain SUM-6218 is maintained prior to its use in the manufacturing process is provided.
5) The CSF is revised to include any preservatives/stabilizers or anti caking agents added to the product, and their MSDSs are provided.
6) Provide an explanation for the presence of the organisms in body organs for a period longer than 21 days or provide an injection tox/path study for a period over 21 days.
7) Results of testing for ß-exotoxin and mammalian toxicity must be provided to the Agency prior to registration of the product. The procedure to dispose of any unacceptable batches must be described. Also, results of testing for enteric pathogens must be provided.

Registrant's Response (dated 09/27/2012) to the Deficiencies found by the Agency in its review of product chemistry, manufacturing process, and acute toxicity studies of the TGAI *Bt. israelensis* strain SUM-6218.

Deficiency1: The product name and active ingredient content are made to match exactly on the CSF and product label.

Registrant's Response:

Label
The product statement of active ingredient on the product label has been changed to read: *Bacillus thuringiensis* subsp. *israelensis,* Strain SUM-6218* 100.00%. A copy of the changed label has been submitted.
CSF:
The product name on EPA Form 8570-4, CSF, has been changed to read:
Summit® Bti MP, the same as on the product label.

Reviewers' Comment: The % by weight of the TGAI on the CSF should be corrected to 100.00%.

Deficiency2: The deposition of the strain in a recognized microbial culture collection is finalized.

Registrant's Response: Box 10 of the CSF has been changed to read: *Bacillus thuringiensis* (CAS # 68038-71-1) subsp. *israelensis*, Strain SUM-6218, ATCC Ref. No. BAA-2453.

Reviewers' Comment: Acceptable

Deficiency 3: The CSF is revised to give a minimum spore or CFU content per unit weight, or a minimum potency in ITU/mg.

Registrant's Response: The revised CSF states: Contains at least 3.2 billion *Aedes aegypti* Units per pound; contains at least 5.3×10^{11} Colony Forming Units (CFU) per gram.

Reviewers' Comment: Acceptable

Deficiency 4: The information on how the seed culture of *Bacillus thuringiensis israelensis* strain SUM-6218 is maintained prior to its use in the manufacturing process is provided.

Registrant's Response: [redacted]

Reviewers' Comment: Acceptable

Deficiency 5: The CSF is revised to include any preservatives/stabilizers or anti caking agents added to the product, and their MSDSs are provided.

Registrant's Response: [redacted]

Reviewers' Comment: The registrant needs to remove any statement of using any preservatives/ stabilizers or anti caking agents from the manufacturing process.

Deficiency 6: Provide an explanation for the presence of the organisms in body organs for a period longer than 21 days or provide an injection tox/path study for a period over 21 days.

Registrant's Response: Amended Intravenous Injection Toxicity and Infectivity Study: Acute Injection Toxicity/Infectivity in Rats has been amended. Under Quantification Significance, from p. 12 through 15, clearance graphs with 95% confidence intervals are presented which demonstrate clearance trends in all respective tissues. P–values are given for clearance in each tissue. One-way ANOVA was performed. It has been noted that: "No abnormalities were seen during daily observations or at necropsy. There was no mortality in any group during the study." At 21-days post-treatment, the mean body weights of the untreated control group was 318.8 g, the inactive MPCA (microbial pest control agent) was 320.6 g, and the MPCA treatment mean was 310.7 g, which all contribute to demonstrate no adverse effects to the test animals by this test material.

Reviewers' Comment: Acceptable

Deficiency 7: Results of testing for ß-exotoxin and mammalian toxicity must be provided to the Agency prior to registration of the product. The procedure to dispose of any unacceptable batches must be described. Also, results of testing for enteric pathogens must be provided.

Registrant's Response:

β-exotoxin Test:

Mouse Subcutaneous Injection Test:

[redacted]

Reviewers' Comment: Acceptable

Disposal of Unwanted Fermentation Beer/Broth:

[redacted]

Reviewers' Comment: [redacted]

Destruction of a Batch of Primary Powder by Summit Chemical Co.:

[redacted]

Reviewers' Comment: Acceptable

Testing for Enteric Pathogens:

[redacted]

Reviewers' Comment: The registrant has to test production batches of the TGAI for contamination with pathogenic bacteria, particularly for the presence of enteric pathogens.